

Metabolism

All chemical & energy transformations.

1) Catabolism

Breakdown of Large molecules
Release of (work, heat or stored) Energy

2) Anabolism

Formation of
Uptake of

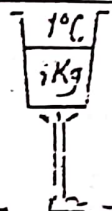
$$\text{Efficiency} = \frac{\text{Work done}}{\text{Total energy}} \times 100$$

isometric cont. 0%

isotonic cont. upto 50%

Calorie C (big or kilo C) :

Heat needed to raise temp. of 1 Kg of H_2O $1^\circ C$



Heat (caloric) value of FOOD
1 gram

Energy equivalent of O_2
1 Litre

Physical CV

outside body

4.1 C

9.3 C

5.3 C

CHO

FAT

Pro

Physiological CV

inside body

4.1 C

9.3 C

4.1 C

completely
oxidised to
nitric acid

N_2
17%

partially
oxidised to
urea

Food

CHO

FAT

Pro

Mixed

EE of O_2

5 C

4.7 C

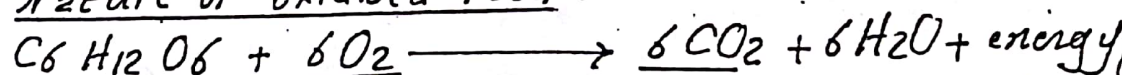
4.5 C

4.8 C

Respiratory quotient (RQ)

- Definition Ratio of volume of CO_2 produced / unit time
volume of O_2 consumed
- Measurement Whole body or individual organ
- Significance

1) Nature of oxidised food :



①

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<u>Food</u>	<u>RQ</u>	
<u>CHO</u>	1	e.g. brain
<u>Fat</u>	0.7	e.g. DM & prolonged starvation
<u>Protein</u>	0.82	
<u>Mixed diet</u>	0.85	

② Type of food (fuel) used by an organ:
 e.g. brain 0.97 - 0.99 principle fuel is CHO

Respiratory exchange ratio (R) same ratio as RQ

<u>RQ</u>	<u>R</u>
- affected only by metabolism - ranges from 0.7 to 1	- affected by other factors - 0.5 or less after exercise due to high O_2 consumption more than 1 in ① Hypervent. : $\uparrow \uparrow CO_2$ wash ② During exercise: $lactic\ acid + NaHCO_3 \rightarrow H_2CO_3 \begin{matrix} \swarrow CO_2 \\ \searrow H_2O \end{matrix}$ ③ Metabolic acidosis: as exercise

Metabolic rate MR

● Definition Energy production per unit time (hour)

● Measurement

$$MR = \frac{O_2 \text{ litres consumed per hour}}{250 \text{ ml/min} \times 60 / 1000} \times \text{EE of } O_2 \times 4.8$$

● Metabolic rate is increased by 3 Es

Exercise, Eating (food intake) & Exposure to cold

Basal metabolic rate BMR

● Definition: MR under basal conditions. $\neq$ 3 Es

① Complete physical & mental rest
 for at least $\frac{1}{2}$ Hour without sleep

②

② Post absorptive state

12-14 hours after the last meal to avoid SDA

③ Comfortable temperature neither shivering nor sweating

BMR is the unavoidable cost of living

i.e. metabolic activity of heart, respiratory muscles & liver

BMR is not the minimal energy expenditure as it -- 10% by sleep

- Normal standard for average size man $40 \text{ C/hour/meter}^2 \pm 15\%$

Clinically BMR is expressed as % deviation from normal

i.e. 60 C/hour/m^2 in average size man is expressed as $+50\%$

- Factors affecting MR:

Physiological:

- BMR is 7% less in ♀ (less muscles & more fat)

- MR is increased by:

3 Es exercise eating exposure to cold

Growth

Pregnancy & lactation

MR is decreased by:

Sleep,

Fasting.

decline with age

Pathological: MR is ++ by

1 ++ body temp i.e. fever.

2 ++ thyroid & adrenal medulla hormones.

3 Malignancy & polycythemia.

Specific dynamic action SDA

- Definition Obligatory energy expenditure due to Food metabolism in LIVER.

- 30% of caloric value of Pro is wasted as SDA

6%

"

CHO

"

4%

"

Fat

"

- SDA comes from the food itself or from the energy stores

- SDA may last up to 6 hours.

Food intake

- Appetate in hypothalamus is composed of:

	<u>Feeding centre</u>	<u>Satiety centre</u>
<u>Site</u>	Lateral	Medial
	<u>hypothalamus</u>	
<u>Stimulation</u> :	++ eating	cessation of eating
<u>Destruction</u> :	Petal anorexia	Hyperphagia & obesity

Polypeptides that regulate appetite:

++ Food intake

Neuropeptide Y

Melanin concentrating hormone

MCH

Ghrelin

-- Food intake

x MSH

Cocaine & amphetamine regulated

transcript (CART)

Corticotropin-releasing hormone CRH

- 4 main hypotheses controlling food intake:

① Lipostatic hypothesis

Leptin (thin) from fat cells x amount of fat.

Leptin acts on the hypothalamus to:

a. Decrease food intake by:

1 -- neuropeptide Y.

2 ++ x MSH.

b. Increase energy expenditure by

++ activity of uncoupling plus

(Leptin receptors on brown fat)

Leptin acts as a feedback by which

Body fat regulates food intake

② Gut hypothesis

Food in GIT releases polypeptide hormones (GRP, glucagon, somatostatin & CCK) which inhibit Feeding centre.

CCK has central (more important) & peripheral receptors

③ Glucostatic hypothesis

++ blood glucose → ++ activity of glucostats of the satiety centre → inhibits Feeding centre and vice versa.

Evidence 1 Hypoglycemia is an appetite stimulant.

2 Polyphagia in DM is caused by failure of satiety centre to utilize glucose with insulin deficiency

(4)

④ Thermostatic hypothesis

-- body temp. below a given set point stimulates appetite

• Other factors that affect food intake:

- ① Sight, smell & taste of food may ++ or -- food intake.
- ② Distension of GIT inhibits appetite.
while contraction of an empty stomach (hunger cont) ++ appetite.
- ③ Brown fat:
 - Small percentage of total body fat (more in infant).
 - Site between the scapulae & at the base of neck along greater vessels in thorax & abdomen.
 - A special form of fat with extensive sympathetic innervation.
Stim. of symp → release noradrenaline via β_3 adrenergic receptors → ++ lipolysis & ++ fatty acid oxidation in mitochondria → ++ heat production i.e. more efficient utilization of food & more energy.
 - Brown fat cells contain many mitochondria that have:
 - a. usual inward proton conductance that generate ATP
 - b. a 2nd proton conductance does not generate ATP but depends on an uncoupling protein (UCP) so it generates more heat & less ATP.

Note Two components of heat production after eating:

- SDI
- Slower ++ heat production caused by symp stim. to brown fat after eating

Obesity

most common nutritional problem

- Body mass index Body weight in Kg / square height in meters
- 25 overweight → 30 more → obese.

- Causes ① Positive energy balance
i.e. energy intake > energy expenditure
- ② Genetic factor
- ③ Hypothalamic factor

- ④ endocrinal factor mainly hypothyroidism
- ⑤ -- sensitivity to leptin.

Complications

- ① Atherosclerosis
- ② Gall Bladder diseases
- ③ Type 2 DM
- ④ Psychological problem
- ⑤ Joint diseases (osteoarthritis & flat foot)

Management

- ① Negative energy balance: (-- food intake & ++ energy output)
- ② Drugs: -- appetite, -- fat absorption or ++ energy output
- ③ Surgical procedures: liposuction.

Body temperature

- Rectal (core) temp. $37^{\circ}\text{C} \pm 0.5$ is constant
 41°C : convulsion occurs.
 43°C : ptn denaturation & death.
- Skin (shell) temp varies with atmospheric temp
 34°C Head, chest & abdomen skin 28°C skin of hands & foot

Physiological variations in body temp:

- ① Diurnal (circadian) rhythm: lowest at morning highest at afternoon
- ② Age: higher in children Unstable in premature babies (incubator at 38°C)
- ③ Sex: Higher in σ ++ 0.5°C in ϕ luteal phase (morning)
- ④ ++ emotions & exercise.
- ⑤ -- prolonged recumbency & starvation.

Regulation of body temp

- ① Ways of heat gain (heat production)
 - Ⓐ BMR & SDA
 - Ⓑ Increased muscle activity:
 - ① Increased muscle tone ++ MR 100%

② Shivering

- Acute exposure to cold

[Centre : Post. part of hypothalamus.

[Innervation : Extrapyramidal (hemiplegic side shivers)
Extrapyramidal system activates antagonistic muscles
This is interrupted cyclically by impulses of proprioceptors.

- ++ heat production 8 times 800%.

③ Voluntary Foot stamping & hand clapping

Note Curare causes paralysis of sk muscles $\rightarrow$ hypothermia

④ Hormonal (nonshivering) thermogenesis

Hypothalamus ++ secretion of adrenaline &
 T_3 & T_4 (infants & animals) via TRH.

② Ways of heat loss :

A Non evaporative :

- ① Radiation Most important if atmosp. temp. is $< 33^\circ\text{C}$
At 20°C 70% of heat loss.

Electromagnetic waves (infrared) between objects not in contact

- ② Conduction to object (atoms) in contact.

- ③ Convection in fluid or gases between 2 areas with different temp.

B Evaporative :

- ① Insensible perspiration via Lungs & Skin
At 24°C 50 ml / hour i.e. 1200 ml / day

Each ml (cc) evaporated H_2O causes a loss of 0.6 Kcal.

- ② Sweat Only way to lose heat above 34°C

[Composition : Hypotonic solution

[Mechanism : Active

Acini : secretes isotonic solution

Duct : aldosterone reabsorbs NaCl & secretes K^+

[Centre : Anterior hypothalamus

[Innervation : Sympathetic cholinergic

[Amount : 0.2 - 1 Litre / hour

[Cooling effect : 1 ml evaporated sweat 0.6 Kcal.

Cooling effect ++ by air current & -- by humidity

Thermoregulatory system 3

1 Thermoreceptors :

a Peripheral (skin) receptors

- Ruffini corpuscle & free nerve endings : For heat
- Krause receptors & " " " : For cold.

More cold receptors especially in face & hands

Lateral spinothalamic tract gives collateral from the thalamus to thermostat in hypothalamus

b Central (hypothalamic) receptors

measure brain & blood temperature i.e. core temp.

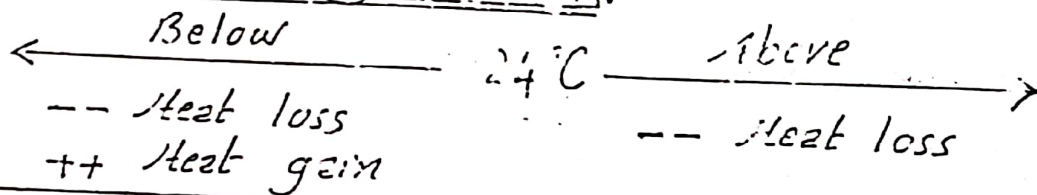
2 Thermoregulatory centre : hypothalamus

Set point 37°C

3 Effector organs :

<u>Items</u>	<u>Below set point</u> <u>Body temp.</u> <u>Above set point</u>	
	<u>Post. part of hypoth.</u> <u>Initiates</u> <u>Anti drop effects</u>	<u>Ant. part of hypoth.</u> <u>Anti rise effects</u>
1 <u>Autonomic</u>	Cutaneous VC symp. adrenergic fibres	1 Cutaneous VD -- symp. tone 2 Sweating (symp) 3 Salivation (parasymp)
2 <u>Somatic</u>	1 ++ muscle tone 2 Shivering 3 Voluntary	Apathy
3 <u>Nervous</u> Limbic lobe	Hunger	Thirst
4 <u>Endocrinal</u>	Adrenaline < ++ HR VC T ₃ T ₄ Glucocorticoids	ADH

Reactions of body to cold:



Increased heat gain via

- [1] Increased muscular activity
 a ++ muscle tone.
 b shivering.
 c Voluntary.

- [2] Hormonal
 a Adrenaline.
 b T_3 & T_4 .
 c Glucocorticoids.

- [3] Behavioural effects
 a ++ Food intake.
 b warm drinks.

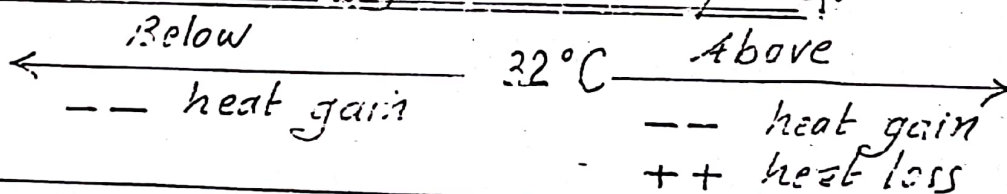
Decreased heat loss via:

- [1] VC of skin vessels
 Most important
 Reaches maximum at 24°C
 $\rightarrow -- \text{temp gradient}$

- [2] Counter-current heat exchanger
 Venous bl. shifts to deep venous plexus
 Heat passes from arterial to blood
 $\rightarrow$ keeps skin temp low
 keeps core temp high

- [3] Behavioural effects
 a Curling of body.
 b Heavy clothes.

Reactions of body to hot atmosphere:



Decreased heat gain via

- [1] VD of skin vessels
 Most important
 Reaches maximum at 32°C
 $\rightarrow +- \text{temp gradient}$

- [2] Behavioural effects
 a Apathy -- movement.
 b Anorexia -- Food intake

Increased heat loss via

Sweating (Discuss)

Acclimatization to cold

++ Adrenaline, T_3 & T_4

Acclimatization to hot

++ sweating & cutaneous VD
 takes 8 to 9 days

This system maintains body temp between $24 - 32^{\circ}\text{C}$

(9)

Disorders of body temperature

① Fever

Toxins of bacteria (endotoxins)
act on monocytes & macrophages (Kupffer cells)
→ release of interleukin I (polypeptide)
known as endogenous pyrogen
stimulates the release of prostaglandins
from the preoptic area of hypothalamus
elevates the set point e.g. 40°C
→ shivering to ++ heat gain

Treatment: Aspirin inhibits prostaglandin synthesis

② Heat stroke In Hot humid atmosphere

Overheating of hypothalamus → paralysis of heat regulating centre

→ -- sweating → ++ body temp.

Symptoms Abdom. distress, vomiting, dizziness, slurred speech

Symptoms are exaggerated by loss of fluids & electrolytes

If plasma denaturation occurs, the condition is irreversible & fatal.

Ut Immersion in cold H_2O & ice to -- body temp.

③ Hypothermia

→ -- metabolism → -- HR, -- ABP & slow respiration

[a] Between $21-24^{\circ}\text{C}$, the process is reversible with gradual cooling
Induced hypothermia is used in brain & cardiothoracic surgery

[b] If hypothermia is severe, it leads to cell freezing

Rewarming should be very gradual & controlled.

Otherwise, cell destruction & death.

Exercise and sport physiology

Metabolic system during exercise

- Primary source of energy :

ATP

Time
3 seconds
of maximal exercise

- Regeneration of ATP :

① Creatine phosphate: CP

CP + ATP = phosphagen system

CP amount 2-4 times ATP

8-10 seconds
of maximal short exercise

② Glucose - lactic acid system

Glycogen $\rightarrow$ Glucose $\xrightarrow{\text{anaerobic}}$ 3 ATP/mol. of glycogen
 $\downarrow$ pyruvate $\rightarrow$ lactic acid which diffuses outside of muscle

2.5 times as rapid as the aerobic system - 1.6 minutes

③ Aerobic (oxidative) system

Glucose $\xrightarrow{O_2}$ 36 ATP

Unlimited source of energy for prolonged activity

Note During marathon race, MR. $\uparrow$ 2000 %

Fuel of exercise

	<u>CHO</u>	<u>FAT</u>
<u>Suits :</u>	brief intense work	slow, prolonged work
<u>Sources :</u>	Only $\frac{1}{2}$ of bl. glucose Muscle & liver glycogen exhausted in 100 min.	fat is the main source Adipose tissue.
<u>Proportions :</u>		
- <u>Maximal</u> exercise	100 %	0
- <u>Submaximal</u> ,,	75 %	25 %
- <u>Moderate</u> ,,	50 %	50 %

So proportion depends on :

① Severity of exercise

② Duration of exercise.

③ Blood level of FFA

④ Training of the individual. (11)

O₂ debt Excess Post Exercise O₂ consumption EPOC

- Definition O₂ consumed post-exercise above basal O₂ consum.
- Functions Refill Hb & Myoglobin with O₂
Reform phosphagen & lactic acid system
- Factors keeping a high EPOC
 - ① ++ body temp.
 - ② ++ Na⁺-K⁺ ATPase to restore electrolyte balance.
 - ③ ++ Catecholamines, T₃ & T₄.

Physiological response to incremental exercise

① Metabolic response

- ② O₂ uptake (V_{O₂}) increases until it reaches a maximum or plateau i.e maximum O₂ uptake (V_{O₂} max.)
- ③ Anaerobic threshold where anaerobic metabolism supplements the aerobic system as the exercise intensity is ++ it denotes that lactic acid production has started.

② Respiratory response provides extra O₂ via

- ④ Ventilation ++ linearly with V_{O₂} up to anaerobic threshold. then vent. ++ disproportionately due to stim. by lactic acid.
Mechanism: Initially, both tidal vol. & resp rate ++
Later on, tidal vol. reaches a plateau.

However, resp. rate continues to increase

- ⑤ Diffusion capacity for O₂ increases 3 fold.
Mechanism: perfusion of all pulm. capillaries i.e ++ surface area

③ Cardiac response: provides extra O₂ via

Cardiac output ++

Mechanism HR ++ linearly with V_{O₂} (Maximum HR 220/min)

SV ++ from 70 to 110 ml/beat then plateaus at V_{O₂} max.

Note in 40% of people, ++ CO depends on ++ HR.

CO reaches more than 90% of its maximum in incremental exercise
Pulm. vent. reaches only 65% of its
So, CO (CVS) is the limiting factor for ++ O₂ consumption

4) Arterio-venous O_2 difference ($A-V$) O_2

$A-V O_2$ ++ allowing more O_2 delivery to tissues due to:

- Redistribution of blood flow $\rightarrow$ greater flow to exercising muscles
- High extraction of O_2 by muscles O_2 diss. curve is shifted to Rt
- ++ muscle capill. bl. volume $\rightarrow$ -- distance of O_2 diffusion

5) Endocrinal response

++ GH, T_3 & T_4 & aldosterone.

Physical Fitness

++ tolerance to exercise.

A) Regulatory response

Few weeks

- 1 shift from symp to parasymp
- 2 Redistribution of blood flow.
- 3 Sweating at lower core temp
- 4 ++ sensitivity to insulin

B) Structural response

Months or years

- 1 ++ skeletal muscle mass
 - 2 ++ cardiac muscle mass
 - 3 ++ bone density
- All with parallel ++ in capillaries

Physiological adaptation to regular training in body systems

1) Metabolic and cellular adaptation

(a) ++ $\dot{V}O_2$ max. 5-30%.

(b) ++ aerobic power by

- 1 ++ myoglobin
 - 2 ++ activity of enzymes of Krebs cycle & mitochondria.
 - 3 ++ fat utilization thus sparing glycogen & glucose for anaerobic activity & delaying hypoglycemic fatigue
 - 4 Muscle fibres: hypertrophy ++ myofibrils number, mitochondrial size, ++ ATP, CP, glycogen & triglycerides
- Result: delay in anaerobic threshold, -- lactic acid $\rightarrow$ delayed fatigue

(c) ++ anaerobic power by ++ activity of enzymes of glycolysis

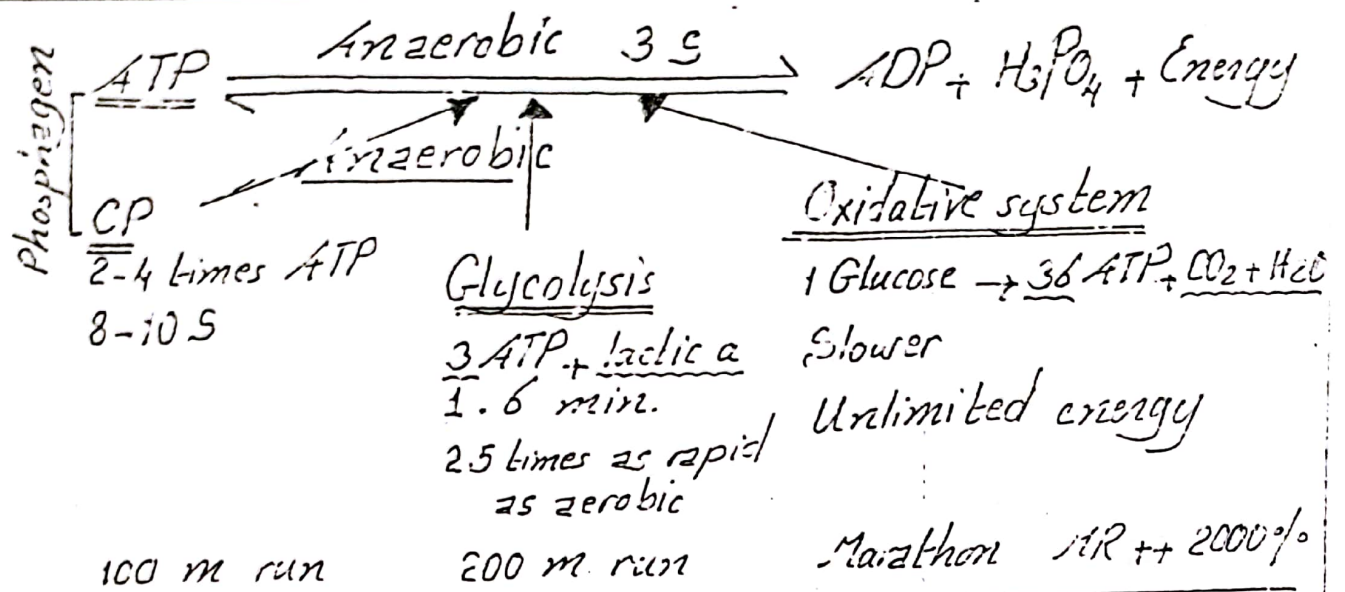
2) Respiratory adaptation

Slower & deeper breathing at rest & during exercise

$\rightarrow$ -- respiratory minute volume due to: 3

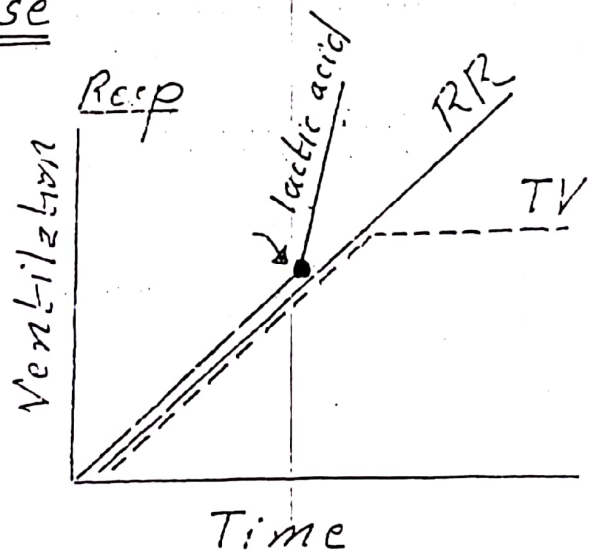
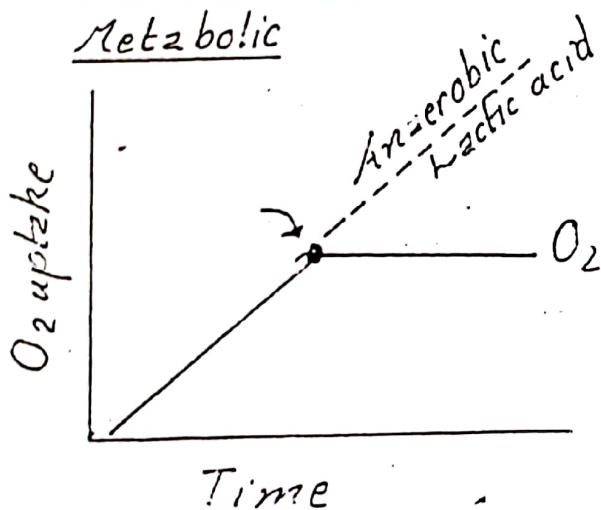
- (1) ++ mechanical efficiency
- (2) Centrally mediated -- ventilatory drive in moderate exercise

(13)

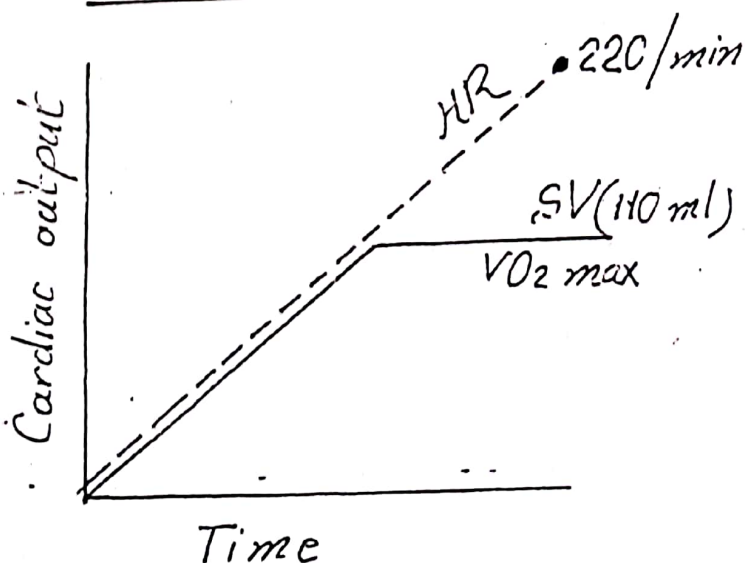


Incremental exercise

Metabolic



Cardiac



40% of people ++ HR only
 In incremental exercise
 CO reaches 90% of its max.
 Pulm vent " 65% of its max
 So, CVS is limiting factor
 For O₂ consump.

METABOLISM

Metabolism is all chemical & energy transformations that occur in the body.

It includes:

1- Catabolism:

It is breakdown of large molecules with release of energy.

This energy is used for maintaining body functions, digesting & metabolizing food, thermoregulation and physical activity.

Energy output = external work + energy storage + heat.

Energy is stored by forming energy rich compounds.

Efficiency = work done / total energy expended.

- Isotonic contractions perform work at peak efficiency 50 %
- In isometric contraction, all energy appears as heat.

2- Anabolism:

It is formation of large molecules with uptake of energy.

To study metabolism, the following are some units, uses & definitions:

1- Calorie:

It is the amount of heat energy necessary to raise the temperature of 1 gm of water 1 degree C.

However, the unit commonly used in physiology & medicine is the big calorie C (kilocalorie): Kcal that equals 1000 calorie (small calorie).

2- Heat value (caloric value) of food:

The amount of heat energy liberated when 1 gm of a certain food is oxidized.

It depends on:

- a- Type of food.
- b- Whether food is oxidized outside the body (physical caloric value) or inside the body (physiological caloric value):

Type of food	Physical CV	Physiological CV
1 gm carbohydrate	4.1 C	4.1 C
1 gm fat	9.3 C	9.3 C
1 gm protein	5.3 C	4.1 C

Carbohydrate & fat are completely oxidized in the body to $\text{CO}_2 + \text{H}_2\text{O}$. Proteins are incompletely oxidized in the body to urea, nitrogenous compounds, CO_2 & H_2O to avoid formation of nitric acid.

3- Energy equivalent of oxygen (E.E. of O₂):

It is the amount of heat in C produced when one liter of O₂ is used to oxidize food substances.

Food substance	E.E. of oxygen
Carbohydrate	5 C
Fat	4.7 C
Protein	4.5 C
Mixed diet	4.8 C

Respiratory quotient (RQ)

Definition:

It is the ratio of volume of CO₂ produced to volume of O₂ consumed / unit time.

$$RQ = \frac{\text{Volume of CO}_2 \text{ produced}}{\text{Volume of O}_2 \text{ consumed}} / \text{unit time.}$$

Measurement:

RQ can be measured for individual organs & for the whole body.

Significance of RQ measurements:

1- It indicates the nature of food substance oxidized:

RQ of carbohydrate is 1.0 & RQ of fat is 0.7

This is because H & O are present in carbohydrates in the same proportions as in water; where as in fat, extra O₂ is necessary for the formation of H₂O.

RQ of protein is 0.82

During prolonged starvation & in untreated diabetes mellitus, the RQ is 0.7 indicating that fat is the chief source of energy under these conditions. If RQ is 0.85, this indicates that an equal mixture of carbohydrates & fats are being utilized.

2- It indicates the type of fuel used by an organ:

RQ of the brain is regularly 0.97 – 0.99 indicating that it's principal but not its only fuel is carbohydrate.

Respiratory exchange ratio (R):

R is the same ratio as RQ.

RQ is affected only by metabolism.

while R is affected by other factors other than metabolism.

RQ ranges from 0.7 to 1.0 according to metabolism.

R can reach 0.5 or less after exercise due to high oxygen consumption.

R can be more than 1 as in:

- a- Hyperventilation due to increased expired CO_2 .
- b- During exercise due to increased production of CO_2 from buffered lactic acid produced during anaerobic glycolysis.
- c- In metabolic acidosis because respiratory stimulation causes the amount of expired CO_2 to rise.

Metabolic rate (MR)

Definition:

It is the rate of energy production / unit time (hour).

Measurement:

O_2 liters consumed by hour X energy equivalent of O_2

$\text{MR} = 250 \times 60 \times 4.8 / 1000 = 74 \text{ C / hour.}$

250 ml = is the volume of O_2 consumed / minute.

4.8 is the energy equivalent of O_2 of a mixed diet.

MR is increased by 3 E:

- 1- Exercise.
- 2- Eating.
- 3- Exposure to cold.

Basal metabolic rate

Definition:

It is the MR measured under the following basal conditions:

1- Complete physical & mental rest for at least 1/2 hour but without sleep.

2- Post- absorptive state:

12 – 24 hours after the last meal to avoid specific dynamic action (SDA) of food.

3- Comfortable temperature:

Neither cold nor hot (neither shivering nor sweating).

BMR is the **unavoidable cost of living** i.e. the energy needed for the metabolic activities of the heart, respiratory muscles, liver & muscle.

BMR is **not the minimal energy expenditure** as it decreases during sleep by about 10 % due to decreased muscle tone.

Since heat exchange occurs at the body surface, the BMR is better expressed / unit surface area i.e. $\text{C / hour / m}^2 \text{ surface area.}$

In an average size man, it is about $40 \text{ C / hour / m}^2 \pm 15 \%$ i.e. about 2000 C / day .

Clinically, BMR is expressed as % deviation from normal e.g. if it is $60 \text{ C / hour / m}^2$ in an average size man, then it is $+ 50 \%$.

Factors affecting the metabolic rate:

Physiological factors:

MR is less in females by 7% (more fat & less muscles).

Increase MR	Decrease MR
1- Muscular exercise. 2- Recent food ingestion. 3- Low environmental temperature. 4- Growth. 5- Pregnancy & lactation.	1- Sleep. 2- Fasting. 3- MR declines with age.

Some pathological factors that increase MR:

- 1- Increased body temperature.
- 2- Increased thyroid hormones.
- 3- Increased epinephrine & norepinephrine.
- 4- Malignancy & polycythemia.

Specific dynamic action (SDA) of food

Definition:

It is the obligatory energy expenditure that occurs during assimilation of food into the body.

It differs according to the type of food.

30 % of the caloric value of protein is wasted as SDA.

6 % of the caloric value of carbohydrate is wasted as SDA.

4 % of the caloric value of fat is wasted as SDA.

SDA comes from the food itself or from the energy stores.

SDA may last up to 6 hours.

SDA is caused by the metabolic process of the food in the liver.

Control of food intake

Role of the hypothalamus:

Appetate is composed of 2 centers:

Feeding center	Satiety center (acts by inhibiting the feeding center)
Lateral hypothalamus.	Medial hypothalamus
Its stimulation → increase eating	Its stimulation → cessation of eating
Its destruction → fetal anorexia	Its destruction → hyperphagia & obesity.

The principal hypothalamic polypeptides that appear to play a role in the regulation of appetite for food include:

Increase food intake	Decrease food intake
Neuropeptide Y	α melanocyte stimulating hormone (α MSH).
Melanin – concentrating hormone (MCH)	Cocaine & amphetamine – regulated transcript (CART).
Ghrelin	Corticotropin releasing hormone (CRH).

The 4 main hypotheses are involved in the control of food intake:

I- The lipostatic hypothesis:

Leptin (thin) that is produced primarily from fat cells in proportional to the amount of fat.

Leptin acts on the hypothalamus to:

1- Decrease food intake by:

- a- Decrease neuropeptide Y.
- b- Increase the activity of α MSH secreting neurons.

2- Increase energy consumption

Mechanism:

Leptin receptors are present in brown adipose tissues & there is evidence that leptin increases the activity of uncoupling proteins thus producing a direct peripheral increase in energy expenditure i.e. leptin acts as humoral signal that operates as a feedback loop by which the size of the body's fat depots to regulate food intake.

II- The gut hypothesis:

Food in the GIT → release of polypeptides that act on the hypothalamus to inhibit food intake.

They include GRP, glucagon, somatostatin & CCK.

Gut peptides may provide short- term, meal to meal control of food.

CCK has both central & peripheral receptors.

Central CCK receptors seem to be more important in producing the anorectic effect (--- appetite).

III- The glucostatic hypothesis:

Increased blood glucose level produces a sensation of satiety.

Mechanism:

Increased activity of the glucostats of the satiety center that in turn inhibits the feeding center & vice versa.

Evidence:

a- Hypoglycemia is an appetite stimulant.

b- Polyphagia is seen in diabetes mellitus, in which blood glucose is high but cellular utilization is low because of the insulin deficiency.

IV- The thermostatic hypothesis:

A fall in body temperature below a given set point stimulates appetite & vice versa.

Evidence:

Food intake is increased in cold weather & decreased in warm weather.

Other factors that affect food intake:

1- Distension of the GIT inhibits appetite while contractions of an empty stomach (hunger contractions) stimulate appetite.

2- Sight, smell & taste of food also affect food intake.

This depends on past experience related to cultural & environmental factors.

3- Brown fat:

A special form of body fat that has an extensive sympathetic innervation. It makes up a small percentage of total body fat & is more abundant in infants.

It is located between the scapulas, at the nape of the neck, along the great vessels in the thorax & abdomen and in other scattered locations.

Brown fat cells contain many mitochondria that have:

a- The usual inward proton conductance that generates ATP.

b- A second proton conductance that does not generate ATP that depends on an uncoupling protein (UCP).

It causes uncoupling of metabolism & less generation of ATP, so that more heat is produced.

Stimulation of the **sympathetic innervation** to the brown fat releases norepinephrine that acts via β_3 -adrenergic receptors to increase lipolysis & increased fatty acid oxidation in the mitochondria that increases heat production.

Thus a variation in the activity in nerves to brown fat produces variations in the efficiency with which food is utilized & the energy produced. They provide a mechanism for varying the weight gained / unit of food ingested.

There are 2 components to the heat production after eating:

a- SDA.

b- The somewhat slower increase in heat produced by brown fat due to increased sympathetic discharge to brown fat after eating.

Obesity

Obesity is the most common & the most extensive nutritional problem.

Energy balance:

It is the balance between caloric intake & energy output.

Body mass index:

Body weight in Kg / squared height in meters.

Values above 25 are abnormal.

25 – 30 are overweight.

More than 30 are obese.

Causes of obesity:

- 1- Excess energy intake than energy expenditure (heat & work) i.e. positive energy balance.
- 2- Genetic factors.
- 3- Hypothalamic factors.
- 4- Endocrinal factors mainly hypothyroidism.
- 5- Decreased sensitivity to leptin.

Complications of obesity:

- 1- Accelerated atherosclerosis.
- 2- Increased incidence of gall bladder disease.
- 3- Increased incidence of joint disease (osteoarthritis) & flat feet.
- 4- Its association with type 2 diabetes (insulin resistance).
- 5- Psychological problems.

Management of obesity:

- 1- Decrease energy intake (restrict food intake) & increase energy output (increase activity & exercise) to produce a negative energy balance is the main line of treatment.
- 2- Drugs that decrease appetite, prevent fat absorption or increase energy expenditure are used,
- 3- Surgical procedures.

Body temperature & its regulation

- In man, the body rectal temperature is kept nearly constant at $37^{\circ}\text{C} \pm 0.6$

- At 41°C , convulsions occur.

- Protein denaturation & death occur at 43°C .

Shell & core temperature

- Skin temperature (shell temperature) is variable in different regions:

Skin of head, chest & abdomen = 34°C

Extremities (hand & feet) = 28°C

Physiological variations in body temperature:

1- Diurnal (circadian) rhythm:

Temperature is lowest in the morning & is highest at the afternoon.

2- Age:

Children have a higher body temperature than adults.

Premature babies possess an immature center for temperature regulation, so they are put in incubators at 38°C .

3- Sex:

It is higher in males than females (more muscles & metabolism).

In females, the morning basal body temperature during the luteal phase increases by about 0.5°C .

4- Body temperature increases by emotions & exercise.

5- Body temperature decreases during prolonged inactivity.

Regulation of body temperature

At constant body temperature, heat gain = heat loss.

I) Ways of heat gain (heat production):

Heat is produced by basal metabolic reactions (for maintenance of cell life & body life) in addition to that produced through increased muscle activity & hormonal stimulation.

A- Increased muscle activity:

1- Increased muscle tone.

2- Shivering:

- . It occurs during acute (not prolonged) exposure to cold.
- . Center: posterior part of the hypothalamus.
- . Innervation: extrapyramidal system activates antagonistic groups of muscles, which is interrupted cyclically by impulses from the muscle proprioceptors.
- . It increases the heat production 8 times.

3- Voluntary:

Foot stamping & hand clapping.

N.B. Curare causes paralysis of skeletal muscles → hypothermia.

B- Hormonal or non – shivering thermogenesis:

The hypothalamus ++ secretion of:

- 1- T3 & T4 (in infants & animals) via TRF.
- 2- Adrenaline.

II) Ways of heat loss:

A- Non – evaporative heat loss:

1- Radiation:

It is the heat transfer by electromagnetic waves between objects that are not in contact.

At 20 °C, it accounts for 70 % of heat loss.

2- Convection:

It is the heat transfer by molecular movement of gasses or liquids between 2 different temperatures.

This transfer can be increased by air currents.

3- Conduction:

It is heat exchange between atoms or molecules in contact with each other.

B- Evaporative heat loss:

- Each 1 cc evaporated sweat causes a loss of 0.6 K.cal.
- At 24 °C (external temperature), 50 ml of H₂O is evaporated by insensible perspiration from the skin & lungs: 30 K.cal / day.

Sweat secretion

- Composition:

It is hypotonic solution.

- Mechanism:

It is an active process;

The acini secrete an isotonic secretion.

In the ducts, aldosterone makes the sweat hypotonic by reabsorption of NaCL.

- **Nerve supply of sweat glands:**

Sympathetic cholinergic fibers (blocked by atropine).

- **Center:**

The anterior portion of hypothalamus.

- **Cooling effect of sweat:**

Sweat secretion starts when environmental temperature is 32 – 34°C, and it is the only way of heat loss above 34°C.

Sweat evaporation is helped by movement & by dry air currents.

- **Amount:**

0.2 – 1 liter are lost by sweating per hour depending on the external temperature.

The thermoregulatory system

It is composed of:

- 1- Thermoreceptors.
- 2- Central integrator: thermoregulatory center.
- 3- Effector organ systems.

Thermoreceptors

1- Peripheral skin receptors:

They measure skin temperature.

Ruffini corpuscle & free nerve endings for heat.

Krause receptors & free nerve endings for cold.

Site:

A large number of cold receptors are present in the face & hands while they are less in the chest & legs.

Pathway:

Impulses pass along the lateral spinothalamic tract to the thalamus & then to the sensory cortex.

Collaterals from the thalamus pass to the thermoregulatory center in the hypothalamus.

2- Central hypothalamus receptors:

They are present in the hypothalamus.

They measure brain & blood temperature i.e. core temperature.

Thermoregulatory center

- **Site:** in the hypothalamus.

- **Its set point:** 37°C.

a- When the body temperature is **below** the set point, the **posterior** part of the hypothalamic center initiates anti – drop mechanisms e.g. VC, shivering, adrenaline & T4 secretion.

b- When body temperature is **above** the set point, the **anterior** part of hypothalamic center initiates anti – rise mechanisms e.g. VD & sweating).

The effector (efferent) organ system is composed of:

Items	Antidrop effects	Anti-rise effects
1) <u>Autonomic impulses</u>	1- Cutaneous VC symp. adrenergic fibres	1- Cutaneous VD - - symp. tone 2- sweating symp. cholinergic fibres 3- ++ Salivation in animal. (only parasymp effect)
2) <u>Somatic impulses</u>	1- Voluntary contraction 2- ++ Muscle tone 3- Shivering	
3) <u>Limbic lobe</u>	1 Hunger	1 Thirst
4) <u>Neuro-endocrine impulse</u>	1- Adrenaline (Calorigenic action & VC) 2- T3 & T4 3- Glucocorticoids	1 Antidiuretic hormone

Reaction of the body during exposure to cold

There is increased heat loss by non – evaporative mechanisms due to higher body temperature than the atmosphere.

The reaction of the body:

The body tries to decrease heat loss & to increase heat production.

A) If the external temperature is not less than 24 °C, the body reacts by decreased heat loss only via:

1- Vasoconstriction of skin vessels:

- The decrease in skin temperature decreases the temperature gradient between the skin & the outside.
- VC of the skin vessels reaches its maximum at 24 °C.

2- Counter – current heat exchange in the skin:

- Venous blood flow is shifted to the deep venous plexuses (vena comitantes). So, the heat is transferred from arterial to venous blood.
- Cooling of arterial blood helps to keep the skin temperature low.
- Warming of venous blood helps to keep the core temperature high.

3- Behavioral responses:

- Putting on heavy clothes.
- Curling of the body to decrease the surface area.

B) If the external temperature is below 24 °C, the body reacts by increased heat gain in addition to decreased heat loss:

1- Increased muscular activity:

- Involuntary: increased muscle tone & shivering.
- Voluntary: clapping of hands & high stepping.

2- Hormonal:

Thermogenesis by adrenaline & T4.

3- Behavioral responses:

Increased food intake & warm drinks.

Reactions of the body during exposure to heat

In external atmospheric temperatures of 32 °C or above:

The non – evaporative heat loss stops.

The body gains heat from the atmosphere by radiation.

Therefore when the temperature is above 32 °C, a decrease in heat gain & sweat secretion are the only effective methods.

A) If the external temperature does not exceed 32 °C, the body reacts by decreasing heat gain via:

1- Vasodilatation of skin vessels:

- Decreased sympathetic impulses, increases bloods flow to the skin & venous blood is shifted to the superficial skin vessels.
- The rise of skin temperature decreases heat gain.
- VD of skin vessels reaches its maximum at 32 °C.

2- The heat production is decreased to the basal level by:

- i. Decreased movement (lethargy & apathy).
- ii. Decreased food intake (anorexia).

B) Increased heat loss:

It starts if the external temperature is above 32 °C by sweat secretion (discuss).

Acclimatization to environmental conditions

These are changes that help to adapt to prolonged exposure to heat or cold.

A) Acclimatization to heat:

Through an increase in the rate of sweating & Cutaneous VD, this mechanism takes 6 – 9 days.

B) Acclimatization to cold:

Through an excessive secretion of T3, T4 and adrenaline.

This system is responsible for the maintenance of body temperature within the normal range (37 ± 0.6 °C) when the external temperature is between 24 – 32 °C.

Abnormal body temperature changes

*** Fever:**

It is hyperthermia due to resetting of the set point of hypothalamus to a higher level.

*** Pathogenesis of fever:**

Toxins of bacteria (endotoxins) act on the monocytes, macrophages, including Kupffer cells leading to their release of interleukin I, interleukin I (polypeptide

known as endogenous pyrogen) stimulates the preoptic area of the hypothalamus to cause endogenous production of prostaglandins. Prostaglandins elevate the set point of hypothalamus to a higher level. So, antidiap responses occur (VC and shivering) to elevate body temperature to the new set point.

Treatment: Aspirin, which prevents prostaglandin synthesis.

Heat stroke

There is limit to heat loss even with maximal sweating.

Moreover, when the hypothalamus becomes extensively heated, its heat regulating ability is depressed & sweating diminishes or stops.

As a result, the body temperature rises.

This happens upon exposure to high temperatures especially in humid air.

Symptoms of heat stroke:

Dizziness, abdominal distress, vomiting & eventually loss of consciousness.

The symptoms are exacerbated by excessive loss of fluid & electrolytes in sweat.

Hyperpyrexia is also damping to body tissues especially the brain.

The condition is fatal unless rapidly treated by cooling measures to decrease the body temperature.

Hypothermia

It is the abnormal drop of core temperature below the normal range.

- Severe skin & blood cooling leads to a lower temperature & metabolism & physiological processes slow down.

Respiration & heart rate are very slow.

Blood pressure is low.

- If the drop is between 21 – 24 °C, the process is reversible if the body is warmed again gradually.

Induced hypothermia is used in the brain & cardiothoracic surgery.

- If hypothermia is severe & leads to cell freezing.

Rethawing (warming) if not very gradually & controlled, it leads to cell destruction & death.

EXERCISE AND SPORT PHYSIOLOGY

The body metabolism increases to 2000 percent during a marathon race.

*Metabolic systems during exercise:

ATP is the primary source of energy for muscle contraction.

ATP stored in muscle is only sufficient for 3 seconds of maximal muscle contraction.

Three different metabolic mechanisms are responsible for reconstituting a continuous supply of ATP in the muscle fibers:

1) Creatine phosphate (CP):

- It is another high energy phosphate compound.
- Muscle cells have 2-4 times as much CP as ATP.
- The cell CP plus ATP are called the phosphagen energy system, which can provide maximal muscle contraction for a period of 8-10 seconds.
- It is used for maximal short bursts of muscle power.

2) The glucose -lactic acid system:

- In the absence of oxygen; glycogen $\longrightarrow$ glucose $\longrightarrow$ pyruvate & 3 mol of ATP / mole of glycogen.
- In the absence of oxygen; most pyruvic acid is converted to lactic acid which diffuses out the muscle into the interstitial fluid & blood.
- Accumulation of acid metabolites within the muscle inhibits further breakdown of glycogen and may interfere with the muscle contractile process.
- This system provides ATP moles 2.5 times as rapid as the oxidative mechanisms of the mitochondria.
- It can provide 1.3 -1.6 minutes of maximal muscle activity in addition to 8-10 seconds provided by the phosphagen system.

3) The aerobic system:

- In the presence of oxygen, pyruvic acid enters the mitochondria and reacts with oxygen to give a net yield of 36 moles of ATP/mol of glucose.
- It is unlimited source of energy (as long as nutrients last).
- It is required for prolonged athletic activity.

***Fuel of exercise:**

1) Carbohydrate: (glycogen & blood glucose):

- The total glycogen store in muscles and liver can be exhausted in 100 minutes of vigorous activity.
- The blood glucose reserve is limited & only half of this source can be used before hypoglycemic problems arise. So, athletes ingest glucose solutions while exercising to counter hypoglycemia and to delay muscle glycogen depletion.
- Carbohydrates are best suited for brief bouts of intense work since it can be used anaerobically.

2) Fats:

- Fat in adipose tissue is the main energy reserve of the body.
- The relative use of carbohydrates & fats during exercise depends on:
 - a- **The intensity of exercise.**
 - In submaximal activity carbohydrate provides 75% of the fuel.
 - Almost all the fuel is glucose at near maximal exercise.
 - With moderate work 50-60% of the energy is derived from fat.
 - b- **The duration of exercise:**
Prolonged steady activity of moderate intensity favors fat usage.
 - c- **Blood levels of fatty acids.**
 - d- **The state of training of the individual.**

***Oxygen debt: (Excess Post - exercise oxygen consumption EPOC):**

Definition: It is the oxygen consumed post-exercise above the resting or basal oxygen consumption.

Functions:

- 1- Refill of Hb & myoglobin with O₂.
- 2- Reconstitute phosphagen and lactic acid system.

Factors keeping a high post-exercise oxygen consumption:

1. Increased body temperature.
2. Increased Na-K ATPase activity after exercise to restore the electrolyte balance.
3. Increased catecholamines and thyroid hormones.

***Physiological response during incremental exercise (Exercise of increasing intensity):**

1 - Metabolic response:

- To increase oxygen consumption during exercise the respiratory system must provide more oxygen, the cardiac system must distribute more blood to the active muscles and the muscle metabolic systems must utilize this increased oxygen provided.
- **Oxygen uptake (VO_2)** increases until it reaches a maximum or plateau [maximum oxygen uptake ($VO_{2\text{ max.}}$)].
 $VO_{2\text{ max}}$ denotes the point at which an individual cannot increase his oxygen consumption anymore.
- As the intensity of exercise increases we reach **anaerobic threshold** where anaerobic metabolism supplements the aerobic system in producing energy. Anaerobic threshold denotes that lactic acid production has started.

2- Respiratory response:

- Extra amounts of oxygen are provided to the blood during exercise through:
 - a- **Ventilation increases linearly with respect to oxygen uptake (VO_2) up to the anaerobic threshold**, then it starts to increase disproportionately compared to oxygen uptake due to lactic acid production which stimulates ventilation. The increase in ventilation is caused initially by an increase in both tidal volume and respiratory rate. However as exercise increases tidal volume reaches a plateau and the increase is then only due to increasing respiratory rate.
 - b- A **three fold increase in oxygen diffusing capacity** resulting due to perfusion of all pulmonary capillaries i.e. greater surface area for oxygen diffusion.

3- Cardiac response:

- **Cardiac output (CO) increases** during exercise to pump more blood to the exercising muscles.
- The heart rate increases linearly with oxygen uptake, while stroke volume increases early during exercise from about 70 ml/beat to 110 ml/beat where it plateaus at $VO_{2\text{ max}}$. In 40% of the individuals then increase in CO depends on the increase in heart rate. The maximum heart rate allowed is 220 / minute.

N.B. The cardiovascular system is the limiting factor for increasing oxygen consumption because the CO reaches more than 90% of its maximum during maximal exercise in contrast to 65% of maximum for pulmonary ventilation.

4- Arterial - venous oxygen content difference (A-V) O₂:

It is widened during exercise allowing more oxygen delivery to the tissues due to:

- a- Changes in distribution of regional blood flow leading to greater flow to the actively exercising muscles.
- b- Local muscle extraction is high due to changes in the tissue environment, which affect the oxygen dissociation curve.
- c- The increased muscle capillary blood volume reduces the average distance for oxygen diffusion.

5- Endocrinal response:

Exercise increases growth hormone, thyroxine and aldosterone blood levels.

Physical fitness:

Physiological adaptations, which allow improved tolerance to the stress of exercise.

A-Regulatory response: rapid develops within few weeks of training.

It includes:

- Shift from sympathetic to parasympathetic activity.
- Redistribution of blood flow.
- Initiation of sweating at a lower core temperature.
- Increased sensitivity to insulin allowing an improved glucose tolerance at lower insulin levels.

B- Structural response: slow, continues for months or years. It includes an increased muscle mass, cardiac tissue and bone with parallel increase in capillary blood supply.

***Physiological adaptations to regular physical training in different body systems:**

1- Metabolic and cellular adaptations:

- a- Increased maximum oxygen consumption, 5-30%.
- b- Increased anaerobic power by increasing the activity of the enzymes of glycolysis.
- c- Increased aerobic power by:
 - Increasing myoglobin levels in active muscles.
 - Increasing the activity of kreb's cycle & mitochondrial respiratory chain enzymes.

d- Fuel usage, increasing fat utilization thus sparing glycogen and glucose for anaerobic activity and delaying hypoglycemic fatigue.

e- Muscle fiber changes: mainly hypertrophy with increased myofibrils, number and size of mitochondria, stored ATP, CP, glycogen and triglyceride levels.

All these metabolic adaptations allow a better aerobic power and is denoted by a *delay* in anaerobic threshold which means the accomplishment of higher exercise intensities without the use of anaerobic metabolism, this also reflects a *lesser* lactic acid level and thus fatigue is delayed.

2- Respiratory adaptation:

Slower and deeper pattern of breathing, both at rest and during exercise with a lesser respiratory minute volume. This reflects three main adaptations:

a- An increase in *mechanical efficiency* thus lowering the oxygen cost of a given work output.

b- A centrally mediated decrease in *ventilatory drive* in moderate exercise.

c- Reduction of the sensitivity of the *carotid chemoreceptors* and a lesser increment of lactate in severe effort.

3- Cardiac adaptation:

- Even though the heart of an athlete is larger than that of a normal person, resting cardiac output is almost the same due to large stroke volume at a reduced heart rate i.e. the heart pumping effect is 40-50% greater in athletes & the increase in CO during exercise depends more on the *increase in stroke volume rather than on heart rate*.

- *Cardiac hypertrophy* is due to overload to the ventricles for a long time each day.

Cardiac hypertrophy is associated with an increase in cross-section of the major coronary arteries, an increase in capillary density and an increase in myocardial perfusion.

- The decrease in heart rate in athletes is mainly due to altered autonomic activity with decrease of both catecholamine output and sensitivity.

4- Body composition adaptation:

a) Muscle hypertrophy is induced by vigorous training. The strength of a muscle of a muscle determined by its size, with a maximum contractile force between 3 & 4 Kg/sqcm of muscle cross-sectional area.

b) Adipose tissue:

- Adipose cells are reduced both in size and fat content.

- There is increased sensitivity to B-receptors allowing the liberation of more free fatty acids.
- Serum triglycerides, low-density lipoproteins and cholesterol are reduced.

***Effect of drugs on exercise performance:**

1-Caffeine:

Small amounts of caffeine increase exercise performance.

2- Male sex hormones: (androgens):

Androgens can increase muscle strength, however they cause liver damage and liver cancer. Also, in men it leads to decrease testicular functions & in women, it causes hirsutism and cessation of menses in women.

3-Amphetamine and cocaine:

Experiments have failed to prove any value of these drugs in exercise performance except as a psychic stimulant. Interaction of these drugs with catecholamines released during exercise might cause death mainly due to overexcitability of the heart leading to ventricular fibrillation.

GOOD LUCK